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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/488,491	01/20/2000	Michel F. Levesque	CEDAR 042638	4505

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EXAMINER	
SCHULTZ, JAMES	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 02/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/488,491	LEVESQUE ET AL.	
	Examin r	Art Unit	
	J. Douglas Schultz	1635	

-- Th MAILING DATE of this communication appears on the cover she t with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2002 and 01 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,15,17,19,22,23,27-30,33-36,39,43-45,47 and 49-66* is/are pending in the application.

4a) Of the above claim(s) *17,19,22,23,27-30,33-36,39 and 61-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,15,43-45,47 and 49-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

1. Applicant's response filed October 22, 2002 and December 1, 2003 have been considered. Rejections and/or objections not reiterated from the previous office action mailed August 14, 2001 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Election/Restrictions

3. Applicant's election with traverse of the method of Group I in the paper filed December 1, 2003 is acknowledged. The traversal is on the ground(s) that the claimed cells which result from the methods taught in the claims, and which were restricted from said methods, would possess a phenotype substantially and detectably different from a basal epidermal cell that is transfected with a neural marker gene (the transfected basal epidermal cell was set forth as an example in the restriction of a product identical to the claimed product that would result from a different process, and thus provided rationale for the restriction). In support of the contention that the cell resulting from applicants' process and the hypothetical cell of the restriction are different, applicants argue that the cells of the instant methods would possess neuritic outgrowths, or be GABAergic or dopaminergic, while the hypothetical cell proposed in the

restriction would not. Applicants assert that because the cell resulting from applicants claimed process would possess a different phenotype than the hypothetical cell proposed in the restriction, applicants argue that the restriction between the process and the product made is improper.

This is not found persuasive, the compound claims are not claiming a cell that results from the method per se, but rather claim a cell "having one or more morphological, physiological and/or immunological feature(s) of a neuronal cell produced by the method" (From claim 17). Applicants attention is particularly drawn to the term "having one or more...features". Thus, any cell that has one or more features would be identical to the claimed cell. The hypothetical cell of the example in the restriction would indeed share one feature, thus meeting the claim limitations. Similarly, transfection with GAD65 or GAD67 and related proteins in the synthesis pathway would cause a cell to be GABAergic, while transfection with the cDNA for tyrosine hydroxylase and related proteins in the case of dopamine. Since a hypothetical epidermal cell so transfected has one or more features of the cell produced by applicants method, the product as claimed can be made by another and materially different process (see MPEP § 806.05(f)), and the requirement is still deemed proper and is therefore made FINAL.

This application contains claims 17, 19, 22, 23, 27-30, 33-36, 39, and 61-66, drawn to an invention nonelected with traverse in the paper filed December 1, 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 49, and by dependency claims 50-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 49 at the end of step "(c)" recites a "a cell having one or more... features of a neuronal;". The term "neuronal" is presumably describing the word "cell", which appears to be absent. Insertion of the word "cell" after "neuronal" would be remedial.

5. Claims 1-11, 15, 43-45, 47, and 49-60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of transdifferentiating epidermal basal cells in culture, comprising culturing a cell population, exposing the cell culture to an antagonist of bone morphogenetic protein (BMP), and an antisense to the mRNA of either human MSX-1 or human HES-1, or a homologous non-human counterpart of either of these, and growing the cells in a combination of growth factors.

The two elements at issue here are a) the breadth of the genus of BMP antagonists, and b) the breadth pertaining to "a homologous non-human counterpart" of either human MSX-1 or human HES-1. Taking the breadth of BMP antagonists first, the limits of this genus are considerable. For example, there have been 13 BMP homologues identified to date. Applicants claim language encompasses antagonists to all 13. General classes of antagonists to BMP activity include small organic molecules, antibodies, antisense nucleic acids, ribozymes, triple helix RNA, aptamers, peptide inhibitors or active fragments thereof, or combinations of these. While applicants' specification describes five peptide inhibitors of BMP, namely fetuin, noggin, chordin, gremlin, and follistatin, this is merely one class of inhibitor. No teaching of any small organic molecules, antibodies, antisense nucleic acids, ribozymes, triple helix RNA, aptamers, or active fragments of peptide inhibitors have been disclosed outside of the five peptide inhibitors mentioned above.

Applicant is referred to the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov). The following passage is particularly relevant.

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

According to this passage, in order to be considered in possession of the genus of all BMP inhibitors as broadly claimed, applicants must be in possession of a representative sample

of species from the genus, which includes any antagonist to any of the 13 identified BMP molecules, as well as any not yet identified. Because applicants' disclosure identifies only 5 inhibitors from one class of inhibitor, and does not teach any structural or functional information that would allow one of skill to immediately envision other members of the claimed genus, applicants are not considered to be in possession of the genus as broadly recited.

Furthermore, the breadth pertaining to "a homologous non-human counterpart" of either human MSX-1 or human HES-1 is also considered to be extensive. This genus includes any peptide with MSX-1 or HES-1 activity, or active fragments thereof, from any species, including those homologues known or yet to be discovered, or other molecules that are not structurally related but retain some activity of MSX-1 or HES-1. Since applicants have not provided any disclosure of anything other than human MSX-1 and human HES-1 (the sequences of which are not taught in the specification, but rather attributed to Suzuki et al., Development 124:3037 (1971), and Ishibashi et al., The EMBO Journal 13:1799 (1994J), respectively), and further does not teach any structural or functional information that would allow one of skill to immediately envision other members of the claimed genus of any molecule with MSX-1 or HES-1 activity, applicants are not considered to be in possession of homologous non-human counterparts of these genes.

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James Douglas Schultz, PhD